

REMARKS

After amendment, claims 37-66 are presently pending in the present application. Claims 1-36 and 40-41 have been cancelled, claim 37 has been amended and claims 42-66 have been newly added. The amendment to the claims is supported by the originally filed application and claims. The claims have been drafted to reflect the Examiner's view of enablement of specific mutations which have been presented in the application. These have been incorporated into the claims. Note that the claims now are directed to mutations at position 234 (claims 44 and 46), positions 180 and 182 (claims 42, 48, 51) and alterations that enhance resistance to proteolysis by one or more proteases defined by the deletion of amino acids 114-170 (claims 45, 49 and 50). The amendment to the claims finds support in the original application as filed, including the claims and examples. No new matter has been added by way of this amendment.

The Examiner has variously objected to or rejected the originally filed claims of the instant application under 35 U.S.C. §112, first and second paragraphs and §102 for the reasons stated in the August 8, 2006 office action. Applicants will address each of the objections/rejections below.

Claim Objections

Applicants thank the Examiner for the cogent commentary on page 4, in the first full paragraph of the August 8, 2006 office action. Corrections to the claims have duly been made, thus obviating this objection.

The 35 USC § 112, Second Paragraph Rejection

The Examiner has rejected the originally filed claims for the reasons which are outlined in

the office action on pages 4-5. It is respectfully submitted that the amended claim and newly presented claims obviate the Examiner's rejection. It is respectfully submitted that the Examiner's rejection, now has been rendered moot.

The 35 USC § 112, First Paragraph Rejection

The Examiner has rejected the originally filed claims under 35 U.S.C. §112, first paragraph, as being non-enabled for the reasons which are set forth in the office action on pages 5-10. The Examiner has indicated that certain mutants are enabled. Applicants have amended the claims to try to reflect the Examiner's indication of enabled subject matter.

In particular, in the present claims, amendments have restricted the IGFBP-2 mutant claims and nucleic acid claims to either combination of mutations at amino acids at positions 180 and 181, or at amino acid position 234, or to the specific deletion of amino acids 114 through 170. It is submitted that there is sufficient disclosure to enable such claims, and the Examiner appears to agree with that assessment. The method claims are restricted to the use of mutants at amino acid position 234 or 180 and 181, or the deletion between amino acids 114 and 170. It is respectfully submitted that the claims are now enablement by disclosure clearly described in the specification.

Given the teachings of the specification, it is respectfully submitted that the claims are now fully compliant with the requirements of 35 U.S.C. §112, first paragraph.

The §102 Rejection

The Examiner has rejected originally filed claims 1, 18, 35 and 36 as being anticipated by Lucic, et al. for the reasons which are explained in the office action at pages 10-11. Separately, the Examiner has rejected originally filed claims 37-39 as being anticipated by Yamano, et al., US patent no. 7,071,160 (Yamano) for the reasons which are stated in the office action on page 12. For the reasons which are presented hereinbelow, Applicants respectfully submit that the

presently pending claims are not impacted by the references cited against the previously pending claims.

The originally pending claims have been amended to restrict the claimed subject matter to specific mutations within IGFBP-2. None of these mutations are described in Lucic *et al.* Therefore, Lucic, et al. cannot possibly anticipate the presently pending claims.

Lucic *et al.*, was published from work undertaken in the laboratory of the inventor. The paper describes the production of IGFBP-2 using a phagemid vector in *E. coli*. The IGFBP-2 protein was produced as a fusion protein with the g3p, gene III product, to assist in secretion of soluble material into the paraplast. In order to obtain IGFBP-2 without the fusion partner at the N terminus, a protease cleavage site was introduced between the g3p and IGFBP-s. A recognition site for the engineered recombinant H64A subtilisin enzyme was introduced. This methodology is commonly used in recombinant production of proteins and may involve the use of a range of different protease recognition sites and enzymes. H64A subtilisin is not a naturally occurring enzyme and is therefore not relevant to proteolysis of IGFBP-2 in normal and cancer tissues. It is quick clear that Lucic, et al. does not anticipate the presently pending claims.

Turning to the Yamano reference, Yamano does not anticipate presently pending claims 37-39. Amended claims 37 to 39 relate to the use of specific mutations in IGFBP-2. Yamano does not teach those mutations, and does not teach the use of those mutations as defined amended claims 37 to 39.

We also note that Yamano describes the sequence of a protein that belongs to a family once classified as IGF binding protein related proteins. This is not the same as the IGFBP-2 of the present patent application. The IGF binding protein related proteins family shares a small degree of sequence similarity to the N-terminal domain (within the first one third of the protein) of the high affinity IGFBPs 1 - 6. Some members of the

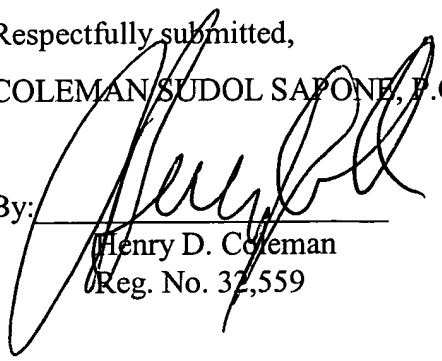
family were shown to have a very low affinity for IGFs (in the order of 1000 fold lower than IGFBP1 - 6). Thus, the prime inventive feature of Yamano is directed to an entirely different protein than that of the present invention. It is respectfully submitted that Yamano does not in any way disclose or suggest the present invention.

Favorable consideration of this application is respectfully solicited.

For all of the above reasons, it is respectfully submitted that the present application is now in condition for allowance and such action is earnestly solicited. 38 claims (including 1 independent claim) have been cancelled and 25 claims (including 2 independent claims for a total of three independent claims pending in the present application) have been added to the present application. No fee is therefore due for the presentation of this amendment.

The Commissioner is authorized to charge any fee or credit any overpayment to deposit account 04-0838.

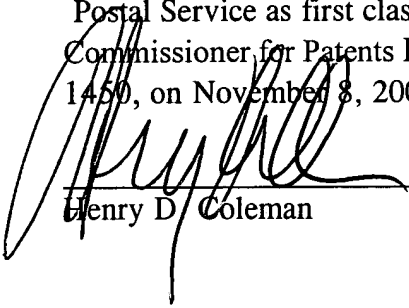
Respectfully submitted,
COLEMAN/SUDOL SAPONE, P.C.

By: 
Henry D. Coleman
Reg. No. 32,559

714 Colorado Avenue
Bridgeport, Connecticut 06605-1601
(203) 366-3560
Dated: 11/08/06

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as first class mail in an envelope addressed to:
Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450, on November 8, 2006.


Henry D. Coleman